APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,470	02/05/2002	David J. Foran	UMNJ-P01-003	1796

			EXAMINER
28120	7590	09/21/2005	LAVIN, CHRISTOPHER L

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

ART UNIT	PAPER NUMBER
2621	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)
Office Action Summary	10/072,470	FORAN ET AL.
	Examiner	Art Unit	
	Christopher L. Lavin	2621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on <u>25 July 2005</u>.

2a) ☒ This action is **FINAL.**   2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) <u>1-28</u> is/are pending in the application.

     4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) <u>1-28</u> is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on <u>20 May 2002</u> is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

     a) ☐ All   b) ☐ Some * c) ☐ None of:

         1. ☐ Certified copies of the priority documents have been received.

         2. ☐ Certified copies of the priority documents have been received in Application No. _____.

         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

     * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>02/14/05</u>.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set
> forth in section 102 of this title, if the differences between the subject matter sought to be patented and
> the prior art are such that the subject matter as a whole would have been obvious at the time the
> invention was made to a person having ordinary skill in the art to which said subject matter pertains.
> Patentability shall not be negatived by the manner in which the invention was made.

2.   The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

    1.   Determining the scope and contents of the prior art.
    2.   Ascertaining the differences between the prior art and the claims at issue.
    3.   Resolving the level of ordinary skill in the pertinent art.
    4.   Considering objective evidence present in the application indicating
            obviousness or nonobviousness.

3.   This application currently names joint inventors. In considering patentability of

the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g)

prior art under 35 U.S.C. 103(a).

4.   Claims 1, 4 – 14, 17 – 24, and 26 – 28 are rejected under 35 U.S.C. 103(a) as

being unpatentable over Soenksen (6,711,283) in view of Zhou (6,633,659).

5.   In regards to claim 1, Soenksen discloses a method comprising:

Capturing an image of a tissue microarray at a first magnification, i.e., resolution, the tissue microarray including a plurality of disks, each disk including a sample of biological specimen (figure 4; col. 7, lines 12 – 16; col. 19, lines 10 – 12);

Locating a first group of disks from the plurality of disks using one or more visual features of the first group of disks (col. 20, lines 57 – 61: Normal and abnormal cells are two different possible groupings for the disks. These cells are identified by using one or more visual features.);

Identifying a grid defined by the first group of disks (col. 17, lines 8 – 10: Calibration markings are used in the method, which are similar to grid lines);

Locating a second group of disks from the plurality of disks using the identified grid to locate disks which do not include the one or more visual features of the first group of disks (col. 20, lines 57 – 61);

Capturing an image of each one of the first group of disks and second group of disks at a second magnification, i.e., higher resolution, (col. 19, lines 12 – 15); and

Storing the captured images (In figure 1, Soenksen discloses a memory (36) for storing captured images).

Soenksen discloses in lines 8 – 10, column 17 that calibration markings are used. Soenksen however, does not disclose using gridlines in the fashion described in these claims, nor is information from the first group used to locate a second group.

6.   Zhou teaches in the paragraph starting at column 10, line 47 that grid lines are identified on the microarray. These grid lines are used both to separate groups and to

identify disks, which are located at grid line intersection points (refereed to as grid point). Zhou discloses grid points in the paragraph starting at column 13, line 30. It should be noted that in the same paragraph Zhou discloses using templates to identify disks. Finally in the paragraph starting at column 14, line 15 Zhou discloses that the identified grid is used "to aid in fixing the locations of other probable sub-grids whose exact positions in their respective sub-grid regions remain uncertain".

7.   Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use grid lines, including a method to find those grid lines, to both identify disks and to use previously located grid lines to find other grid lines as taught by Zhou along with the method for imaging microarrays as disclosed by Soenksen. Microarrays consist of samples in a grid pattern, by using those grid lines the accuracy in finding and evaluating disks in the method disclosed by Soenksen could be increased.

8.   In regards to claim 4, Soenksen in view of Zhou discloses the method of claim 1 wherein locating the first group of disks comprises convolving the image of the tissue microarray with a disk template that includes the one or more visual features (Soenksen, col. 20, lines 57 – 61; Zhou, col. 13, lines 32 – 34: One particular visual feature used in the template is the diameter of the disks. Using a template to identify a disk would make an excellent first pass to identify disks that are of interest, this would be a way of speeding up the method disclosed by Soenksen as well as improving reliability.).

9.   In regards to claim 5, Soenksen discloses the method of claim 1 further

comprising quantitatively analyzing the captured images of each one of the first group of

disks and the second group of disks to obtain quantitative data (Soenksen, in figure 4

that upon imaging the microarray the image is analyzed (step 214); Soenksen, col. 20,

lines 57 – 61: During analysis quantitative data is obtained.).

10.   In regards to claim 6, Soenksen discloses the method of claim 5 further

comprising storing the location and the quantitative data for each one of the first group

of disks and the second group of disks in a database (Soenksen, col. 13, lines 14 – 17:

Imagery data is available for viewing over a network.   Inherently some form of data

storage is needed to allow the imagery data to be available to a network. Official notice

is taken that it is well known in the art that a database is an efficient means of storing

data structures especially when there are many copies of a data structure.   As the

method disclosed by Soenksen will most likely be used on many microarrays there will

be many microarray data structures that will need to be stored, a database is the most

likely and best means to provide storage.).

11.   In regards to claim 7, Soenksen discloses the method of claim 6 further

comprising providing access to the database over a network to one ore more remote

clients (Soenksen, col. 13, lines 14 – 17).

12.   In regards to claim 8, the method of claim 1 wherein capturing the image of the

tissue microarray at the first magnification, i.e., resolution, further comprises combining

a plurality of portions of the tissue microarray (Soenksen, figure 4, step 202: The

microarray is captured as series a of line images. Those line images are then assembled into one image in step 212).

13.   In regards to claim 9, Soenksen the method of claim 1 wherein a robotic microscope, i.e., scanner, is employed to capture the image of the tissue microarray and to capture the image of each one of the first group of disks and the second group of disks (Soenksen, col. 16, lines 41 - 52).

14.   In regards to claim 10, Soenksen discloses the method of claim 1 wherein the robotic microscope, i.e., scanner, is accessible over a network (Soenksen, col. 21, lines 3 - 7).

15.   In regards to claim 11, Soenksen discloses the method of claim 1 wherein the method is performed by a robotic microscope, i.e., scanner, under control of a computer program without user intervention to autonomously capture and archive magnified images of each disk in the tissue microarray (Soenksen, col. 12, lines 35 – 39; Soenksen, col. 16, lines 41 – 52).

16.   In regards to claim 12, Soenksen discloses the method of claim 11 further comprising autonomously analyzing each captured image and storing a result of each autonomous analysis (Soenksen, col. 16, lines 41 – 52; storage has already been previously discussed).

17.   In regards to claim 13, Soenksen discloses the method of claim 1 wherein the one or more visual features include matching to a disk template (Soenksen, col. 20, lines 57 – 61; Zhou, col. 13, lines 32 – 34).

18.   In regards to claim 14, claim 14 is rejected for the same reasons as those used

to reject claim 1. The argument is analogous to that presented above for claim 1, and

therefore the rejection to claim 1 is equally applicable to claim 14.

19.   In regards to claim 17, claim 17 is rejected for the same reasons as those used

to reject claim 4. The argument is analogous to that presented above for claim 4, and

therefore the rejection to claim 4 is equally applicable to claim 17.

20.   In regards to claim 18, claim 18 is rejected for the same reasons as those used

to reject claim 5. The argument is analogous to that presented above for claim 5, and

therefore the rejection to claim 5 is equally applicable to claim 18.

21.   In regards to claim 19, claim 19 is rejected for the same reasons as those used

to reject claim 6. The argument is analogous to that presented above for claim 6, and

therefore the rejection to claim 1 is equally applicable to claim 19.

22.   In regards to claim 20, claim 20 is rejected for the same reasons as those used

to reject claim 9. The argument is analogous to that presented above for claim 9, and

therefore the rejection to claim 9 is equally applicable to claim 20.

23.   In regards to claim 21, Soenksen discloses a system comprising:

        Capturing means, i.e., scanner 11, for capturing an image of tissue microarray at

a first magnification, i.e., resolution, the tissue microarray including a plurality of disks,

each disk including a sample of a biological specimen (figure 4; col. 7, lines 12 – 16; col.

19, lines 10 – 12).

        First locating means for locating a first group of disks from the plurality of disks

using one or more visual features of the first group of disks (col. 20, lines 57 – 61:

Normal and abnormal cells are two different possible groupings for the disks. These
cells are identified by using one or more visual features.);

Identifying means for identifying a grid defined by the first group of disks (col. 17,
lines 8 – 10: Calibration markings are used in the method, which are similar to grid
lines);

Second locating means for locating a second group of disks from the plurality of
disks using the identified grid to locate disks which do not include the one ore more
visual features of the first group of disks (col. 20, lines 57 – 61);

The capturing means further for capturing an image of each one of the first group
of disks and the second group of disks at a second magnification, i.e., resolution (col.
19, lines 12 – 15); and

Storing means for storing the captured images (In figure 1, Soenksen discloses a
memory (36) for storing captured images).

Soenksen discloses in lines 8 – 10, column 17 that calibration markings are
used. Soenksen however, does not disclose using gridlines in the fashion described in
these claims, nor is information from the first group used to locate a second group.

24.   Zhou teaches in the paragraph starting at column 10, line 47 that grid lines are
identified on the microarray. These grid lines are used both to separate groups and to
identify disks, which are located at grid line intersection points (refereed to as grid
point). Zhou discloses grid points in the paragraph starting at column 13, line 30. It
should be noted that in the same paragraph Zhou discloses using templates to identify
disks. Finally in the paragraph starting at column 14, line 15 Zhou discloses that the

identified grid is used "to aid in fixing the locations of other probable sub-grids whose exact positions in their respective sub-grid regions remain uncertain".

25.   Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use grid lines, including a method to find those grid lines, to both identify disks and to use previously located grid lines to find other grid lines as taught by Zhou along with the system for imaging microarrays as disclosed by Soenksen. Microarrays consist of samples in a grid pattern, by using those grid lines the accuracy in finding and evaluating disks in the system disclosed by Soenksen could be increased.

26.   In regards to clam 22, Soenksen discloses in figure 1 a computer (44) and an imaging device (11). Soenksen discloses in the paragraph starting at column 13, line 14 that the imaging device is controlled by the computer. The imaging device is designed to take images, which are sent to the computer for processing. As shown in previous rejections the system is designed for imaging microarrays. In lines 30 – 36 on column 21 Soenksen discloses that particular areas can be selected for imaging, this requires a specific location, in the same grouping of lines a high resolution is disclosed which requires that the system be provided with a specific magnification. The rest of this claim has been dealt with in claims 1 and 4. Please see these claims for reasons of rejection.

27.   In regards to claim 23, Soenksen discloses the system of claim 22 wherein the computer communicates with the imaging device through a local area network (Soenksen discloses in figure 1 a network 42 for the computer 44 to communicate with the imaging system 11).

28.   In regards to claim 24, Soenksen discloses the system of claim 22 wherein the computer communicates with the imaging device through an internetwork (Soenksen, col. 13, lines 7 – 10).

29.   In regards to claim 26, Soenksen discloses the system of claim 22 further comprising a database for storing, for each disk of the first group of disks and the second group of disks, and image of the disk, a location of the disk, and a quantitative analysis of the disk (Soenksen, col. 13, lines 14 – 17: Imagery data is available for viewing over a network. Inherently some form of data storage is needed to allow the imagery data to be available to a network. Official notice is taken that it is well known in the art that a database is an efficient means of storing data structures especially when there are many copies of a data structure. As the system disclosed by Soenksen will most likely be used on many microarrays there will be many microarray data structures that will need to be stored, a database is the most likely and best means to provide storage.).

30.   In regards to claim 27, Soenksen discloses the system of claim 26 wherein the database is accessible from one or more remote computers through an internetwork (Soenksen, col. 13, lines 14 – 17)

31.   In regards to claim 28, The method of claim 1 wherein said one or more visual features comprises one or more visual shape features (col. 20, lines 57 – 61: A morphological algorithm is an algorithm for determining shape features.).

32. Claims 2, 3, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soenksen (6,711,283) in view of Zhou (6,633,659) as applied to claims 1 and 14 above, and further in view of Sugiyama (5,616,905).

33. In regards to claim 2, Soensken (as modified by Zhou) discloses identifying grid lines. However Soensken (as modified by Zhou) does not disclose using a Hough transform to identify these grid lines.

34. Sugiyama teaches in the paragraph starting at column 11, line 34 that a Hough transform can be used to identify grid lines.

35. Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use a Hough transform to identify grid lines. Hough transforms are well known as excellent line finding operations. As grid lines are by definition lines, using a Hough transform is a fast an efficient way to find the grid lines.

36. In regards to claim 15, claim 15 is rejected for the same reasons as those used to reject claim 2. The argument is analogous to that presented above for claim 2, and therefore the rejection to claim 2 is equally applicable to claim 15.

37. In regards to claim 3, Soensken in view of Zhou and further in view of Sugiyama discloses the method of claim 2 wherein locating a second group of disks comprises selecting locations at one or more intersections which do not include any of the first group of disks (As previously disclosed in the rejection of claim 1 grid points are used to find disk locations. So every disk is located at an intersection of grid lines. Also as disclosed in the rejection of claim 1, Soensken discloses identifying two types of disks, abnormal and normal cells.).

38.   In regards to claim 16, claim 16 is rejected for the same reasons as those used to reject claim 3. The argument is analogous to that presented above for claim 3, and therefore the rejection to claim 3 is equally applicable to claim 16.

39.   Claims 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Soenksen (6,711,283) in view of Zhou (6,633,659) as applied to claim 22 above, and further in view of Caroll (6,121,960).

40.   In regards to claim 25, Soenksen (as modified by Zhou) discloses in figure 1 a step of interactively reviewing an image (step 216). This step inherently requires a user interface. Soenksen (as modified by Zhou) however, does not disclose using a voice-activated command system for interfacing with this user interface.

41.   Carrol teaches in the paragraph staring at column 3, line 53 that a voice-activated command system can be used for interfacing with a user interface.

42.   Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use a voice-activated command system with the user interface disclosed by Soenksen. In a clutered lab a voice-activated interface might save space by eliminating a keyboard and mouse while allowing users who are not computer savvy the ability to use the system disclosed by Soenksen.

Response to Arguments

43.   Applicant's arguments filed 07/25/05 have been fully considered but they are not persuasive.

44.   Applicant argues that Soenksen does not disclose the step of "locating a first group of disks from the plurality of disks using one or more visual features of the first group of disks".

The disagreement seems to be focused on col. 20, lines 57 – 61. Based on the applicant's arguments it seems the problem lies in the phrase "normal or abnormal cells". It appears the applicant is taking this to mean that only one of the two types is identified. It is first pointed out that by identifying one type of cells all the other cells are immediately identified as a second group of cells which are not the first group. Soenksen in the same section also states that "to identify and locate specific types of objects". This phrase allows for multiple types to be identified. Thus both abnormal and normal may be identified on the same sample.

45.   Applicant next argues that Soenksen does not teach capturing at a higher resolution.

It appears to the examiner that applicant is keying in on the words "each one of" and is arguing that Soenksen only captures part of the image at higher resolution. First it is noted that Soenksen does not state that the selected areas can not encompass the entire sample which would thus capturing every cell. Second in the same paragraph Soenksen discloses that the entire sample can be captured at high resolution, this again would encompass all of the cells.

46.   Applicant argues that Soenksen does not disclose a grid.

As the examiner wrote a 103 partially based on the fact that Soenksen does not disclose a grid it is clear the examiner agrees. The examiner was merely pointing out

that Soenksen discloses a similar concept, that of calibration markings. Both calibration markings and grids are designed to help an imaging system accurately determine coordinates.

47.   The applicant argues that Zhou does not teach "locating a second group of disks from the plurality of disks using the identified grid to locate disks which do not include the one or more visual features of the first group".

First it should be noted that the step can be written in the following fashion: "locating a second group of disks, which do not include the one or more visual features of the first group, from the plurality of disks using the identified grid to locate disks". This is how the examiner understands the claim. Zhou discloses using an identified grid (the grid found with locating a first group) to "aid in fixing the locations of other probable sub-grids whose exact positions in their respective sub-grid regions remain uncertain". Thus a grid is used to locate the disks, Soenken's morphological algorithm would still be required to identify the second group.

48.   Finally the applicant argues that there is no motivation to combine the two references. However the examiner provided motivation as can be seen in the rejection above.

Conclusion

49.   **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within
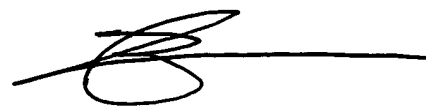
TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher L. Lavin whose telephone number is 571-272-7392. The examiner can normally be reached on M - F (8:30 - 5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mancuso Joseph can be reached on (571) 272-7695. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Lavin

BRIAN WERNER
PRIMARY EXAMINER